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Please find below and/or attached an Office communication concerning this application or proceeding.

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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/697,716
Filing Date: October 31, 2003
Appellant(s): BOSCH, H. WILLIAM

Michele M. Simkin
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed March 15, 2010 appealing from the Office action mailed March 15, 2009.

The appeal brief is filed in the new format under the revised BPAI final rule before the effective date of the BPAI final rule. The Office published the BPAI final rule to amend the rules governing practice before the BPAI in *ex parte* patent appeals. *See Rules of Practice Before the Board of Patent Appeals and Interferences in Ex Parte Appeals; Final Rule, 73 FR 32938 (June 10, 2008), 1332 Off. Gaz. Pat. Office 47 (July 1, 2008)*. However, the effective date for the BPAI final rule has been delayed. *See Rules of Practice Before the Board of Patent Appeals and Interferences in Ex Parte Appeals; Delay of Effective and Applicability Dates, 73 FR 74972 (December 10, 2008)*. In the notice published on November 20, 2008, the Office indicated that the Office will not hold an appeal brief as non-compliant solely for following the new format even though it is filed before the effective date. *See Clarification of the Effective Date Provision in the Final Rule for Ex parte Appeals, 73 FR 70282 (November20, 2008)*. Since the appeal brief is otherwise acceptable, the Office has accepted the appeal brief filed by appellant.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

WITHDRAWN REJECTIONS

The following grounds of rejection are not presented for review on appeal because they have been withdrawn by the examiner. Upon further consideration, the Examiner has decided to withdraw the Obviousness Double Patenting (ODP) rejection of claims 1, 5-7, 9-14, 17-22, 28-41, and 43-47 over claims 1-31, 36-38, and 40 of co-pending 10/697,703 and the ODP rejection of claims 1, 5, 9, and 13-14 over claims 1-6 of co-pending application 10/317,948.

(8) Evidence Relied Upon

The following is a listing of the evidence (e.g., patents, publications, Official Notice, and admitted prior art) relied upon in the rejection of claims under appeal:

5,145,684	LIVERSIDGE	9-1992
5,916,596	DESAI	6-1999

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claims 1-3, 5-7, 9-14, 17-22, 28-41, and 43-47 are rejected under 35 U.S.C. 103 (a) as being unpatentable over Liversidge et al. (U.S. 5,145,684, previously cited) in view of Desai et al. (U.S. 5,916, 596, previously cited).

Liversidge et al. teach dispersible particles consisting essentially of a crystalline drug substance having a surface modifier adsorbed on the surface thereof in an amount sufficient to maintain an effective average particle size of less than about 400 nm (instant claims 1 and 5; see abstract and col. 2, lines 3-35 and 38-43). Additionally, Liversidge et al. teach pharmaceutical compositions containing the particles which exhibit unexpected bioavailability and that are useful in treating mammals (see abstract, col. 2, lines 35-37 and 57-60, and col. 3, lines 3-5 and 22-24). Moreover, Liversidge et al. teach that poorly soluble drugs tend to have poor bioavailability and thus tend to be eliminated in the gastrointestinal tract and unsafe for intravenous administration (see col. 1, lines 13-27). Furthermore, Liversidge et al. teach that decreased drug particles tend to have increased rate of dissolution (see col. 1, lines 28-34). As a result, Liversidge et al. sought to provide stable dispersible drug particles in the submicron size range which can be readily prepared, do not flocculate, do not require the presence of a crosslinked matrix, and drug particles that are highly desirable in pharmaceutical compositions as they have enhanced bioavailability (see col. 2, lines 22-29). Liversidge

et al. also teach that the invention can be made as a stable dispersion wherein the dispersion medium is water (instant claims 7, 9, and 31; see col. 3, lines 45-50) consisting essentially of the liquid dispersing medium and the above-described particles dispersed therein (see col. 2, lines 44-46). Additionally, Liversidge et al. teach that the particles comprise a drug substance wherein the drug substance exists as a discrete crystalline phase (instant claim 1; see col. 3, lines 32-37). Moreover, Liversidge et al. teach that the invention can be practiced with a wide variety of drug substances especially those that are poorly soluble (see col. 3, lines 38-44). Suitable drug substances can be selected from a variety of classes including anti-inflammatory agents, antivirals, corticosteroids, and the like etc...(instant claims 21-22; see col. 3, lines 53-68 and col. 4, lines 1-27; and col. 15, claims 4-5). Moreover, the drug substance as described above have a surface modifier adsorbed on the surface thereof wherein the most useful modifiers are those that physically adhere to the surface of the drug substance but do not chemically bond to the drug and comprise organic and inorganic pharmaceutical excipients including the anionic surfactants such as sodium dodecylsulfate or sodium lauryl sulfate and bioadhesive surfactants such as hydroxypropylcelluose or polyvinylpyrrolidone (instant claims 13-14 and 17-18; see col. 4, lines 34-68 and col. 5, lines 1-19). Liversidge et al. also teach that close to 90% of the particles have an effective average particle size of 400 nm thereby suggesting that the composition also contain other drug substance particle sizes (instant claims 19-20 and 28-29; see col. 5, lines 25-40 and col. 15, claims 2-3). Particularly, Liversidge et al. teach that the concentration of the drug substance may vary from 0.1-60% while the

surface modifier can vary from about 0.1 to about 90% with the viscosity of the suspension being less than 1000 cps or less than 1000 mPa•s (instant claims 10-11 and 44-47; see col. 5, lines 64-68; col. 6, lines 1-5 and 25-31; col. 7, lines 10-20; and col. 15, claims 1 and 6). The compositions can include acceptable carriers for parenteral injection, oral administration in solid or liquid form, for rectal administration and the like (instant claim 6; see col. 7, lines 53-60 and col. 8, lines 10-13).

Liversidge et al. do not specifically teach that the drug substance is triamcinolone acetonide. Additionally, Liversidge et al. do not teach addition of at least two surface stabilizers or addition of other drug substances to the composition. Moreover, Liversidge et al. do not teach the redispersibility of the particles or the pharmacokinetic profile of the drug substances including the particular absorption levels and percentages of Tmax, Cmax, AUC or the bioequivalency.

Desai et al. teach compositions containing water insoluble pharmacologically active agents (i.e. poorly water soluble drugs) in which the pharmacologically active agents are delivered in suspended coated particles and wherein the composition is redispersible and readily bioavailable (see abstract). Desai et al. was also provided to demonstrate that the corticosteroid triamcinolone acetonide is a poor soluble drug (instant claims 2-3; see col. 11, lines 1-67, col. 12, 1-67, col. 13, lines 1-67, and col. 14, lines 1-53) and thus would have been obvious to one of ordinary skill at the time of the invention to substitute into the composition of Liversidge et al. since Liversidge et al.

teach the use of poorly soluble drugs and corticosteroids in his composition. Additionally, Desai et al. teach that such compositions can be formulated in various forms including topical forms (see col. 8, lines 17-22).

Additionally, one of ordinary skill in the art would have found it obvious to add additional surface stabilizers and anti-inflammatory agents such as acetylsalicylate to the composition depending on the desired stabilizing effect and the desired composition. Moreover, it is the position of the Examiner that the composition taught by the cited references would have properties similar to that of the claimed invention, because the references teach the use of the same claimed surface modifiers and the same methods of making such particles which would necessarily confer the same enhanced pharmacokinetic profiles observed. It is further noted that products of identical chemical composition cannot have mutually exclusive properties and therefore a chemical composition and its properties are inseparable. Thus, if the prior art teaches the identical chemical structure, the properties disclosed and/or claimed by applicant are necessarily present. *In re Spada, 911 F.2d 705,709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990).*

It is further noted that In re Best,195 USPQ 430, and In re Fitzgerald, 205 USPQ 594, discuss the support of rejections wherein the prior art discloses subject matter which there is reason to believe inherently includes functions that are newly cited or is identical to a product instantly claimed. In such a situation the burden is shifted to

the applicants to "prove that subject matter shown to be in the prior art does not possess characteristic relied on" (205 USPQ 594, second column, first full paragraph).

Regarding the redispersibility of the triamcinolone particles, given that Liversidge in view of Desai teach that the particles do possess minute diameters, the Examiner contends that it would be well within the purview of one of ordinary skill in the art and obvious to one skilled in the art to conclude that the modified particles of Liversidge are able to redistribute to the lung and liver in view of the teachings of Liversidge et al. that the particles do not aggregate or flocculate.

Thus, to one of ordinary skill in the art at the time of the invention would have found it obvious to substitute triamcinolone acetonide as the drug substance into the composition of Liversidge et al. since Liversidge et al. teach that poorly soluble drugs would be effective in his invention and in view of Desai who teaches that corticosteroids such as triamcinolone acetonide are poorly water soluble drugs and that such drugs possess enhanced bioavailability and which possesses the same pharmacokinetic profiles as the drug particles of Liversidge. Thus, given the teachings of Liversidge and Desai, one of ordinary skill would have been motivated to substitute triamcinolone into the composition of Liversidge with the reasonable expectation of providing a topical composition that is readily bioavailable and a composition that does not aggregate.

(10) Response to Argument

A. Rejection Liversidge in view of Desai

(1) Appellants submit that one skilled in the art has to first choose the drug category of corticosteroids out of 40 categories of drugs disclosed by Liversidge and then among all corticosteroids disclosed by Desai further choose triamcinolone. Thus, such references do not suggest preferentially select triamcinolone or the drug category it belongs to

The Examiner disagrees with such argument as the Examiner maintains that the rejection was rendered obvious over Liversidge in view of Desai. Liversidge teaches dispersible particles in the submicron size range of a crystalline drug substance having a surface modifier adsorbed unto such surface. Liversidge teaches that the invention can be practiced with a wide variety of drug substance especially those that are poorly soluble. Additionally, Liversidge discloses various categories of drugs that can be included in the invention *inter alia* corticosteroids. Liversidge does not explicitly disclose the use of triamcinolone. However, Desai teaches compositions containing poorly water soluble drugs wherein such drugs are in the form of coated particles in order to render such drugs redispersible and readily bioavailable. Desai further teach that drugs that contemplated by the invention involve substantially water insoluble active agents including corticosteroids such as triamcinolone acetonide. Thus, the Examiner maintains that in view of KSR, one of ordinary skill in the art would have indeed found it obvious to substitute and obvious to try triamcinolone in the composition of Liversidge since Liversidge provided the motivation to one skilled in the art to choose poor water soluble drugs including corticosteroids in his invention and in view of Desai who explicitly teaches that corticosteroids such as triamcinolone are poor water soluble

drugs. While applicant argues that no preferential suggestion is provided by the references to select triamcinolone, the Examiner contends that in view of KSR one of ordinary skill in the art would have found it obvious to try each and every drug disclosed by Desai and one skilled in the art would have had a reasonable expectation of success since Liversidge suggested the use of poorly soluble drugs and given that Desai teaches the corticosteroid drug, triamcinolone, as a poorly soluble drug. As for applicant's argument that not every combination drugs and surface modifiers is expected to yield the desired results, the Examiner disagrees and refers applicant to the guidelines provided by Liversidge to ensure achievement of the desired results (see Liversidge, col. 7, lines 23-46 and examples 1-14). Thus, because Liversidge provided the suggestion to select poorly water soluble drugs including those from the classes of corticosteroids, and in view of Desai who teaches that the corticosteroid, triamcinolone, is a poorly soluble drug, the Examiner maintains that one skilled in the art would have found it obvious to substitute triamcinolone into the composition of Liversidge.

> (2) Appellants submit that a rejection based on the "obvious to try" rationale must be supported by a reasonable expectation of success. Applicant thus maintains that it has not been established that one skilled in the art would have had a reasonable expectation that a stable nanoparticulate composition comprising triamcinolone can be obtained in view of the lack of predictability in the art.

The Examiner again disagrees as the Examiner contends that a finite number of predictable solutions was indeed provided by the prior art and that Liversidge and Desai provided the guidelines in order to obtain stable, redispersible and bioavailable compositions. The fact that a long list of possible drugs to be incorporated into the

compositions was provided does not preclude one skilled in the art to try each and every single possibility purported by the prior art as long as such solutions are predictable and as long as a reasonable expectation of success exists. In this instance, the Examiner contends that Liversidge provided the motivation to one skilled in the art to choose corticosteroids and poorly soluble drugs while Desai further teach the use of particular corticosteroids that are poorly soluble including triamcinolone. Moreover, Liversidge provided methods by which to achieve successful compositions and how to predict such solutions. As a result, the Examiner maintains that in light of the disclosure of Liversidge and Desai, one of ordinary skill in the art would have indeed found it obvious to substitute and obvious to try triamcinolone into the composition of Liversidge.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

/SREENI PADMANABHAN/

Supervisory Patent Examiner, Art Unit 1627

Conferees:

/Johann R. Richter/

Supervisory Patent Examiner, Art Unit 1616

/Samira Jean-Louis/

Examiner, Art Unit 1627